AMENDMENTS

Please enter the following amendment without prejudice or disclaimer.

In the Specification:

Please insert the following paragraphs after the third paragraph starting on page 4 line 12, and before the fourth paragraph starting on page 4, line 19:

--This invention also provides an isolated human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1.

This invention further provides an isolated human endothelin receptor precursor comprising an amino acid sequence from Met at -20 to Asn at 407 of SEQ ID NO: 1.

This invention further provides a method for identifying an agonist or an antagonist of a human endothelin receptor, comprising the steps of:

contacting a sample comprising human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1, with a candidate compound; and

detecting binding of the candidate compound to the endothelin receptor.

C1

In one embodiment, the candidate compound is detectably labeled, and wherein the step of detecting comprises measuring the amount of label bound to the sample.

In another embodiment, the sample comprises a cell expressing the endothelin receptor.

In another embodiment, the step of detecting comprises measuring a change in a current across the cell membrane.

In one embodiment, the current across the cell membrane increases, and the candidate compound is determined to be an agonist.

In another embodiment, the current across the cell membrane decreases, and the candidate compound is determined to be an antagonist.

In another embodiment, ET-1 or ET-2 is provided to the cell prior to contacting the cell with the candidate compound.

In another embodiment, the cell contains a DNA molecule comprising a nucleic acid sequence from G at 545 to C at 1765 shown in SEQ ID NO: 1.

This invention further provides a method of manufacturing a pharmaceutical composition, comprising the steps of:

screening a library of candidate compounds by:

contacting a sample comprising a human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1 with each candidate compound in the library,

detecting binding of the candidate compound to the endothelin receptor, and

identifying compounds which bind to the endothelin receptor;

selecting a target compound identified from the library; and

formulating said target compound with a pharmaceutically acceptable carrier.

C1 Cont

In one embodiment, the candidate compound is detectably labeled, and the step of detecting comprises measuring the amount of label bound to the sample.

In another embodiment, the sample comprises a cell expressing the endothelin receptor.

In another embodiment, the step of detecting comprises measuring a change in a current across the cell membrane.

In one embodiment, the current across the cell membrane increases, and the target compound is an agonist.

In another embodiment, the current across the cell membrane decreases, and the target compound is an antagonist.

In another embodiment, ET-1 or ET-2 is provided to the cell prior to contacting the cell with the candidate compound.

In another embodiment, the cell contains a DNA molecule comprising a nucleic acid sequence from G at 545 to C at 1765 shown in SEQ ID NO: 1.

This invention further provides a pharmaceutical composition produced by

screening a library of candidate compounds by:

contacting a sample comprising a human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1 with each candidate compound in the library,

detecting binding of the candidate compound to the endothelin receptor, and

identifying compounds which bind to the endothelin receptor;

selecting a target compound identified from the library; and

formulating said target compound with a pharmaceutically acceptable carrier.

C1 Cont

This invention further provides a method of modulating an endothelin receptor, comprising the steps of:

screening a library of candidate compounds by:

contacting a sample comprising a human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1 with each candidate compound in the library,

detecting binding of the candidate compound to the endothelin receptor, and

identifying compounds which bind to the endothelin receptor;

selecting a target compound identified from the library; and

contacting the endothelin receptor with the target compound.

In one embodiment, the candidate compound is detectably labeled, and the step of detecting comprises measuring the amount of label bound to the sample.

In another embodiment, the sample comprises a cell expressing the endothelin receptor.

In another embodiment, the step of detecting comprises measuring a change in a current across the cell membrane.

In one embodiment, the current across the cell membrane increases, and the target compound is an agonist.

In another embodiment, the current across the cell membrane decreases, and the target compound is an antagonist.

In another embodiment, ET-1 or ET-2 is provided to the cell prior to contacting the cell with the candidate compound.

C1 Cont

In another embodiment, the cell contains a DNA molecule comprising a nucleic acid sequence from G at 545 to C at 1765 shown in SEQ ID NO: 1.

This invention further provides a method of treating a condition characterized by abnormal activity of endothelin receptors in a subject, comprising the steps of:

screening a library of candidate compounds by:

contacting a sample comprising a human endothelin receptor having an affinity for endothelins 1 and 2, comprising an amino acid sequence from Asp at 1 to Asn at 407 of SEQ ID NO: 1 with each candidate compound in the library,

detecting binding of the candidate compound to the endothelin receptor, and

identifying compounds which bind to the endothelin receptor;

selecting a target compound identified from the library; and

administering the target compound to the subject.

In one embodiment, the candidate compound is detectably labeled, and the step of detecting comprises measuring the amount of label bound to the sample.

In another embodiment, the sample comprises a cell expressing the endothelin receptor.

In another embodiment, the step of detecting comprises measuring a change in a current across the cell membrane.

In one embodiment, the current across the cell membrane increases, the target compound is an agonist, and the condition is caused by a reduced endothelin receptor activity.

In another embodiment, the current across the cell membrane decreases, the target compound is an antagonist, and the condition is caused by a increased endothelin receptor activity.

C' cont

In another embodiment, ET-1 or ET-2 is provided to the cell prior to contacting the cell with the candidate compound.

In another embodiment, the cell contains a DNA molecule comprising a nucleic acid sequence from G at 545 to C at 1765 shown in SEQ ID NO: 1.

This invention further provides a method of determining ET-1 or ET-2 in a sample, comprising the steps of: